SUPPLEMENTAL AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No.: 09/870,676

IN THE CLAIMS:

Please enter the following amendments and/or additions to the claims:

Claim 1. (Previously Amended) A method for producing a mixed acid anhydride of formula (1):

$$R^1C(O)OY(O)_n(R^2)_p \quad (1)$$

wherein R^1, R^2, Y, n and p denote the same as defined below,

which comprises adding

a carboxylic acid of formula (2);

C1

$$R^1COOH \quad (2)$$

wherein R^1 denotes

a hydrogen atom,

an optionally substituted alkyl group,

an optionally substituted aryl group, or

an optionally substituted hetero ring, and

an organic base to a solution of a carboxylic acid activating agent of formula (3);

$$(R^2)_p Y(O)_nX \quad (3)$$

wherein R^2 denotes

an optionally substituted aliphatic hydrocarbyl group,

an optionally substituted aromatic hydrocarbyl,

an optionally substituted chain or cyclic alkoxy group, or

an optionally substituted aryloxy group,

Y denotes

a carbon atom, a phosphorus atom, or a sulfur atom,

X denotes

a fluorine atom, a chlorine atom, a bromine atom, an iodine atom, a cyano group or a group of formula:

$$(R^2)_p\ Y(O)_nO\text{-},$$

wherein R^2 is the same as defined above,

n and p are an integer of 1 or 2; and

when Y is a carbon atom, n=1 and p=1,

when Y is a phosphorous atom, n=1 and p=2, and

when Y is sulfur atom, n=2 and p=1 and R^2 denotes an optionally substituted alkyl or aryl group.

Claims 2-4 (Cancelled)

Claim 5. (Currently Amended)A method according to claim 1, wherein R^1 denotes

a hydrogen atom, a straight, branched or cyclic (C1-C17)alkyl group, a (C2-C5)alkenyl or (C5-C6)cycloalkenyl group, a (C3-C4) alkynyl group, a phenyl, tolyl, biphenyl or naphthyl group, an aralkyl, arylalkenyl or arylalkynyl group, a pyridyl group, a 1,3-oxazole group, a 1,3-thiazole group, a furyl group, a tetrahydrofuryl group, a thienyl group,

an imidazole or (C2-C11)alkyleneimine group of which nitrogen atoms are protected by a protecting group,

wherein said groups other than hydrogen atom may be substituted with

(a) a hydroxy group or a halogen atom, or

(b) an amino group of formula:

$R^{11}R^{12}N$- and

optionally further with at least one group selected from

C1

a carbamoyl group, a methylmercapto group, a 4-pyrimidinone-3-yl group, an alkyl(C1-C3)dithio group, of which alkyl is substituted with a protected amino and carboxyl groups, a mercapto, guanidyl, carboxyl, hydroxy or imidazolyl group, wherein

R^{11} represents a hydrogen atom or an amino-protecting group,

R^{12} represents an amino-protecting group, or a group of formula: R^{13}-CO,

wherein R^{13} represents a saturated or unsaturated hydrocarbyl group or a hetero ring, which may be substituted with (c) a hydroxy group, or a halogen atom, or a group of formula: $R^{14}R^{15}N$- and optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group, an alkyl (C1-C3) dithio group, of which alkyl is substituted with an amino and carboxyl groups, an amino, mercapto, guanidyl, carboxyl, hydroxy, or imidazolyl group,

wherein R^{14} is an amino-protecting group, and

SUPPLEMENTAL AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No.: 09/870,676

R^{15} represents a hydrogen atom, a saturated or unsaturated hydrocarbyl group, a hetero ring or an amino-protecting group,

provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R^1, R^2, and substituent groups contained therein are in a protected form,

R^2 denotes a chain, branched or cyclic (C1-C6) alkyl group, which may be substituted with a halogen atom, a phenyl which may be substituted with a halogen or (C1-C3) alkyl group, a chain or cyclic (C1-C6) alkoxy group, or a phenoxy group which may be substituted with a halogen or C1-C3 alkyl group.

Claim 6. (Currently Amended) A method according to claim 5, wherein R^1 represents a group of formula (6): $R^{11}R^{12}N$-A- (6)

wherein R^{11} and R^{12} are as defined in claim 5, and A represents an alkylene group, an alkenylene group, an alkynylene group, an arylene group, an aralkylene group, an arylalkenylene group, an arylalkynylene group, an oxazole ring, a thiazole ring, or an imidazole ring.

Claims 7-8 (Cancelled)

Claim 9. (Previously Amended) The method according to claim 1, 17, 18, 19 or 20, wherein said carboxylic acid activating agent of formula (3) is an acid chloride.

SUPPLEMENTAL AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No.: 09/870,676

Claim 10. (Previously Amended) The method according to claim 1, 17, 18, 19, or 20, wherein the amount of the organic base is 0.9 to 2 moles per mol of said carboxylic acid in the production of the mixed acid anhydride of formula (1).

Claim 11. (Previously Amended) The method according to claim 1, 17, 18, 19, or 20, wherein the amount of the carboxylic acid activating agent is 0.95 to 1.05 moles per mol of the carboxylic acid of formula (2).

C1

Claim 12. (Previously Amended) The method according to claim 1, 17, 18, 19, or 20, wherein the amount of the organic base is 0.95 to 1.05 mol per mol of the carboxylic acid of formula (2).

Claim 13. (Previously Amended) The method according to claim 1, 17, 18, 19, or 20, wherein the amount of the organic base per mol of the carboxylic acid of formula (2) is substantially equimolar.

Claim 14. (Previously Amended) The method according to claim 1, 17, 18, 19, or 20, wherein the organic base is N-methylmorpholine.

Claim 15. (Previously Amended) The method according to claim 18, 19, or 20, wherein the base and the carboxylic acid are simultaneously added.

Claim 16 (Cancelled)

SUPPLEMENTAL AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No.: 09/870,676

Claim 17. (Currently Amended) A method for producing a mixed acid anhydride of formula (1):

$$R^1C(O)OY(O)_n(R^2)_p \quad (1)$$

wherein R^1, R^2, Y, n and p denote the same as defined below, which comprises adding

a carboxylic acid of formula (2):

$$R^1COOH \quad (2)$$

C 1 wherein R^1 denotes

a hydrogen atom, a straight, branched or cyclic (C1-C18) alkyl group, a (C2-C5) alkenyl or (C5-C6) cycloalkenyl group,

a (C3-C4) alkynyl group, a phenyl, tolyl, biphenyl or naphthyl group, an aralkyl, arylalkenyl or arylalkynyl group, a pyridyl group, a 1,3-oxazole group, a 1,3-thiazole group, a furyl group, a tetrahydrofuryl group, a thienyl group,

an imidazole or (C2-C11) alkyleneimine group of which nitrogen atoms are protected by a protecting group,

wherein said groups other than hydrogen atom may be substituted with

(c) a hdyroxy group or a halogen atom, or

(d) an amino group of formula:

$R^{11}R^{12}N$- and

optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group, a 4-pyrimidinone-3-yl group, an alkyl (C1-C3) dithio group, of which alkyl is substituted with an amino and carboxyl groups, a mercapto, guanidyl, carboxyl, hydroxy or imidazolyl group, wherein

R^{11} represents a hydrogen atom or an amino-protecting group,

R^{12} represents an amino-protecting group, or a group of formula: R^{13}-CO,

wherein R^{13} represents a saturated or unsaturated hydrocarbyl group or a hetero ring, which may be substituted with (c) a hydroxy group, or a halogen atom, or a group of formula: $R^{14}R^{15}N$- and optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group, an alkyl (C1-C3) dithio group, of which alkyl is substituted with an amino and carboxyl groups, an amino, mercapto, guanidyl, carboxyl, hydroxy, or imidazolyl group,

wherein R^{14} is an amino-protecting group, and

R^{15} represents a hydrogen atom, a saturated or unsaturated hydrocarbyl group, a hetero ring or an amino-protecting group, and

an organic base to a solution of a carboxylic acid activating agent of formula (3):

$(R^2)_pY(O)_nX$ (3)

wherein R^2 denotes

a chain, branched or cyclic (C1-C6) alkyl group, which may be substituted with a halogen atom,

a phenyl which may be substituted with a halogen or (C1-C3) alkyl group,

a chain or cyclic (C1-C6) alkoxy group, or

SUPPLEMENTAL AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No.: 09/870,676

a phenyl group which may be substituted with a halogen or C1-C3 alkyl group,

Y denotes a carbon atom, a phophorus atom, or a sulfur atom,

X denotes a fluorine atom, a chlorine atom, a bromine atom, an iodine atom, a cyano group or a group of formula:

$(R^2)_pY(O)_nO$-,

wherein R^2 is the same as defined above, n and p are an integer of 1 or 2; and when Y is a carbon atom, n=1 and p=1, when Y is a phosphorous atom, n=1 and p=2, and when Y is sulfur atom, n=2 and p=1 and R^2 denotes an optionally substituted alkyl or aryl group,

provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R^1 and R^2 and substituent groups contained therein are in a protected form.

Claim 18. (Currently Amended) A method for producing a mixed acid anhydride of formula (1):

$$R^1C(O)OY(O)_n(R^2)_p \qquad (1)$$

wherein R^1, R^2, Y, n and p denote the same as defined below, which comprises adding a carboxylic acid of formula (2):

$$R^1COOH \qquad (2)$$

wherein R^1 denotes

a group of formula (6): $R^{11}R^{12}N$-A- (6)

wherein ~~R^1~~ R^{11} represents a hydrogen atom or an amino-protecting group, and

R^{12} represents an amino-protecting group, or a group of formula: R^{13}-CO,

wherein R^{13} represents a saturated or unsaturated hydrocarbyl group or a hetero ring, which may be substituted with a hydroxy group, or a halogen atom, or a group of formula: $R^{14}R^{15}N$- and optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group, an alkyl (C1-C3) dithio group, of which alkyl is substituted with an amino and carboxyl groups, an amino, mercapto, guanidyl, carboxyl, hydroxy, or imidazolyl group,

wherein R^{14} is an amino-protecting group, and

C1

R^{15} represents a hydrogen atom, a saturated or unsaturated hydrocarbyl group, a hetero ring or an amino-protecting group,

A represents an alkylene group, an alkenylene group, an alkynylene group, an arylene group, an aralkylene group, an arylalkenylene group, an arylalkynylene group, an oxazole ring, a thiazole ring, or an imidazole ring, and

an organic base to a solution of a carboxylic acid activating agent of formula (3):

$$(R^2)_pY(O)_nX \qquad (3)$$

wherein R^2 denotes a chain, branched or cyclic (C1-C6) alkyl group, which may be substituted with a halogen atom, a phenyl which may be substituted with a halogen or (C1-C3) alkyl group, a chain or cyclic (C1-C6) alkoxy group, or a phenoxy group which may be substituted with a halogen or C1-C3 alkyl group,

Y denotes a carbon atom, a phosphorus atom, or a sulfur atom,

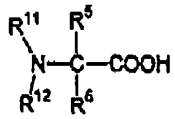
X denotes a fluorine atom, a chlorine atom, a bromine atom, an iodine atom, a cyano group or a group of formula:

$(R^2)_pY(O)_nO$-,

wherein R^2 is the same as defined above, n and p are an integer of 1 or 2; and when Y is a carbon atom, n=1 and p=1, when Y is a phosphorous atom, n=1 and p=2, and when Y is sulfur atom, n=2 and p=1 and R^2 denotes an optionally substituted alkyl or aryl group,

provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R^1 and R^2 and substituent groups contained therein are in a protected form.

Claim 19. (Currently Amended) A method according to claim 17, wherein said carboxylic acid of formula (1) is an α-amino acid derivative of formula (7):

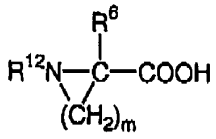


(7)

wherein R^5 and R^6 represent a hydrogen atom or a saturated or unsaturated hydrocarbyl group or a hetero ring, both of which may be each substituted with (a) a hydroxy group or a halogen atom, or (b) at least one group selected from a carbamoyl group, a methylmercapto group, an alkyl (C1-C3) dithio group, of which alkyl is substituted with a protected amino and carboxyl groups, and an amino, mercapto, guanidyl, carboxyl, hydroxy or imidazolyl group, R^{11} is a hydrogen atom or an amino-protecting group, R^{12} represents an amino-protecting group or a group of formula: $R^{13}CO$-, wherein R^{13} represents a saturated or unsaturated hydrocarbyl group or a hetero ring, which may be substituted with (c) a hydroxy or a halogen atom, or (e) a group of formula: $R^{14}R^{15}N$- and optionally further with at least one group selected from a carbamoyl

group, a methylmercapto group, alkyl (C1-C3) dithio group, of which alkyl is substituted with a protected amino and carboxyl groups, an amino, mercapto, guanidyl, carboxyl, hydroxy, or imidazolyl group, wherein R^{14} is an amino-protecting group, R^{15} represents a hydrogen atom or an amino-protecting group, and R^{11} and R^{12}, and R^{14} and R^{15} may independently form an alkyleneimine group, a 4-pyrimidinone-3-yl group or the like, provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R^{11}, R^{12}, R^5 and R^6 or substituent groups contained therein are in a protected form.

Claim 20. (Currently Amended) ~~A method according to claim 19,~~ A method for producing a mixed acid anhydride ~~wherein said carboxylic acid is~~ a cyclic α-amino acid derivative of formula (8):



(8)

wherein ~~R^{12} and R^6 independently denote the same as defined in claim 19, and~~ m denotes an integer from 1 to 10., R^6 represents a hydrogen atom or a saturated or unsaturated hydrocarbyl group or a hetero ring, which may be substituted with (a) a hydroxy group or a halogen atom, or (b) at least one group selected from a carbamoyl group, a methylmercapto group, an alkyl (C1-C3) dithio group, of which alkyl is substituted with a protected amino and carboxyl groups, and an amino, mercapto, guanidyl, carboxyl, hydroxy or imidazolyl group, R^{12} represents an amino-protecting group or a group of formula: $R^{13}CO$-, wherein R^{13} represents a saturated or unsaturated hydrocarbyl group or a hetero ring, which may be substituted with (c) a hydroxy or a

halogen atom, or (e) a group of formula: $R^{14}R^{15}N$- and optionally further with at least one group selected from a carbamoyl group, a methylmercapto group, alkyl (C1-C3) dithio group, of which alkyl is substituted with a protected amino and carboxyl groups, an amino, mercapto, guanidyl, carboxyl, hydroxy, or imidazolyl group, wherein R^{14} is an amino-protecting group, R^{15} represents a hydrogen atom or an amino-protecting group, and R^{14} and R^{15} may independently form an alkyleneimine group, a 4-pyrimidinone-3-yl group or the like, provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R^{12} and R^6 or substituent groups contained therein are in a protected form, and

Sub P1

C1

an organic base to a solution of a carboxylic acid activating agent of formula (3):

$(R^2)_pY(O)_nX$ (3)

wherein R^2 denotes

a chain, branched or cyclic (C1-C6) alkyl group, which may be substituted with a halogen atom,

a phenyl which may be substituted with a halogen or (C1-C3) alkyl group,

a chain or cyclic (C1-C6) alkoxy group, or

a phenyl group which may be substituted with a halogen or C1-C3 alkyl group,

Y denotes a carbon atom, a phophorus atom, or a sulfur atom,

X denotes a fluorine atom, a chlorine atom, a bromine atom, an iodine atom, a cyano group or a group of formula:

$(R^2)_pY(O)_nO$-,

Sub P1

wherein R^2 is the same as defined above, n and p are an integer of 1 or 2; and when Y is a carbon atom, n=1 and p=1, when Y is a phosphorous atom, n=1 and p=2, and when Y is sulfur atom, n=2 and p=1 and R^2 denotes an optionally substituted alkyl or aryl group,

provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R^2 and substituent groups contained therein are in a protected form.

C1

Claim 21. (New) A method according to claim 1, wherein R^1 denotes

a hydrogen atom, a straight, branched or cyclic (C1-C17)alkyl group, a (C2-C5)alkenyl or (C5-C6)cycloalkenyl group, a (C3-C4) alkynyl group, a phenyl, tolyl, biphenyl or naphthyl group, an aralkyl, arylalkenyl or arylalkynyl group, a pyridyl group, a 1,3-oxazole group, a 1,3-thiazole group, a furyl group, a tetrahydrofuryl group, a thienyl group, an imidazole or (C2-C11)alkyleneimine group of which nitrogen atoms are protected by a protecting group,

wherein said groups other than hydrogen atom may be substituted with

(a) a hydroxy group or a halogen atom, or

(b) an amino group of formula:

$R^{11}R^{12}N$- and

optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group, a 4-pyrimidinone-3-yl group, an alkyl(C1-C3)dithio group, of which alkyl is substituted with a protected amino and carboxyl groups, a mercapto, guanidyl, carboxyl, hydroxy or imidazolyl group, wherein

R^{11} represents a hydrogen atom or an amino-protecting group,

R^{12} represents an amino-protecting group, or a group of formula: R^{13}-CO,

wherein R^{13} represents a saturated or unsaturated hydrocarbyl group or a hetero ring, which may be substituted with (c) a hydroxy group, or a halogen atom, or a group of formula: $R^{14}R^{15}N$- and optionally further with at least one group selected from

C1 a carbamoyl group, a methylmercapto group, an alkyl (C1-C3) dithio group, of which alkyl is substituted with an amino and carboxyl groups, an amino, mercapto, guanidyl, carboxyl, hydroxy, or imidazolyl group,

wherein R^{14} is an amino-protecting group, and

R^{15} represents a hydrogen atom, a saturated or unsaturated hydrocarbyl group, a hetero ring or an amino-protecting group,

provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R^1, R^2, and substituent groups contained therein are in a protected form,

R^2 denotes a chain, branched or cyclic (C1-C6) alkyl group, which may be substituted with a halogen atom, a phenyl which may be substituted with a halogen or (C1-C3) alkyl group, a chain or cyclic (C1-C6) alkoxy group, or a phenoxy group which may be substituted with a halogen or C1-C3 alkyl group, provided that the protecting group of the protected amino group, and the amino-protecting group is t-butyloxycarbonyl group.

SUPPLEMENTAL AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No.: 09/870,676

C 1 Claim 22. (New) A method according to claim 5 or 17, wherein the base and the carboxylic acid are simultaneously added.